Docket No.: C15043/174944

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of :	)	
Harold M. Bates	)	Examiner: D. Venci
Serial No.: 10/777,543	)	Art Unit: 1641
Filed: February 12, 2004	)	
For: DETECTION OF ASYMPTOMATIC CORONARY ARTERY DISEASE USING ATHEROGENIC PROTEINS AND ACUTE PHASE REACTANTS	)	

New York, NY
July 22, 2009

TWELFTH SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Mail Stop Amendment
Commissioner For Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Applicant wishes to make of record the following documents (clean copies and Form PTO/SB/08 listing the documents are enclosed). The following documents were cited in the Supplementary European Search Report in European Application No. 05711992.7, which corresponds to the present application. The Supplementary European Search Report, a copy of which is enclosed, was communicated on May 14, 2009, which is less than three months from the date of mailing of this paper (including enclosures).

1. US2003/077668 to Uchida et al., published April 24, 2003 ('Uchida"), entitled "Method For Arteriosclerosis Diagnosis." Uchida concerns "[a] novel method for detecting LDL and denatured LDL (particularly, oxidized LDL) having a significant concerning with [sic] the onset and progress of arteriosclerosis and Alzheimer's disease is provided, wherein a complex of denatured low density lipoprotein (particularly, oxidized LDL) with an acute phase reactant, blood coagulation.fibrinolytic [sic] related protein or disinfectant substance produced by macrophage is used as a measuring subject." (Abstract.) "[T]he present invention has been achieved on the basis of the discovery that the ... complex exists in human blood, not in an arteriosclerosis patient's lesion and that its concentration has a close relationship with the onset and progress of arteriosclerosis." (Paragraph 17.) "[T]he onset and progress of arterioscloerosis is diagnosed by determining whether a concentration of an oxidized LDL/marker protein complex obtained from a patient is significantly higher than that previously obtained from a healthy person." (Paragraph 37, lines 1-5.) "[T]he amounts of oxidized LDL-α1 antitrypsin, oxidized LDL-fibrinogen, oxidized LDL-SAA, oxidized LDL-CRP complexes in the serums of a group of coronary artery disease patients were significantly greater than those of healthy persons." (Paragraph 284; see also paragraph 49 and FIG. 6.)

2. Kwon, K., et al., "Autoantibody against, Malondialdehyde-Modified Low Density Lipoprotein in Patients with Non-Diabetic Unstable Angina: A Potential Role in Immunologic Reaction of Plaque Instability," *Yonsei Medical Journal*, Vol. 43, No. 2, pp. 203-210 (2002) ("Kwon"). Kwon concerns a "study demonstrat[ing] that the plasma levels of autoantibody titer against MDA-modified LDL are significantly elevated

in patients with CAD than control subjects and that these levels are significantly higher in unstable angina than in those with a stable clinical presentation. However, there was no significant difference of the autoantibody titers between the stable angina group and control group. In addition, there was no significant association between the autoantibody titer and the severity of CAD. These data thus show that the increase of antibody reactivity levels against MDA-modified LDL is dependent on the unstable clinical presentation. Therefore, these results suggest that immune response to oxidized LDL may be associated with plaque instability and elevated autoantibody titer might be a useful marker for plaque vulnerability. These results are consistent with previous studies, which indicated that plasma levels of MDA-modified LDL are associated with acute coronary syndromes. However, this study is the first clinical study which demonstrates the association of autoantibody titer against MDA-modified LDL and unstable clinical presentation." (Page 208, left column, first full paragraph (citations omitted); see also FIG. 1B.)

3. Islam, S., et al., "Association of Apolipoprotein A Phenotypes and Oxidized Low-Density Lipoprotein Immune Complexes in Children," *Arch Pediatr Adolesc Med.*, Vol. 153, 57-62 (1999) ("Islam"). Islam concerns a "study to evaluate the relationship of ox-LDL-ab and oxLDL-ICs with known cardiovascular risk factors in children.... This study found either negative correlation or no relationship between ox-LDL-Ab and known cardiovascular risk factors. In contrast, soluble LDL-ICs were significantly correlated with known cardiovascular risk factors." (Page 61, left column, lines 18-31.)

This Twelfth Supplemental Information Disclosure Statement is being filed in accordance with 37 CFR § 1.97(b)(3), before the mailing of a first Office action on the merits. It is believed that no fee is due. If it is deemed that a fee is owing, please charge our Deposit Account No. 02-4467.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on July 22, 2009.

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Respectfully submitted,

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